Shock

Introduction

This lesson is about shock and vasopressors. Those subjects might seem scary. You might not have enough experience yet to even know why it should be scary. This lesson is extremely unlike the well-thought-out experiments that gave us the knowledge that this lesson is based on. If you go to most pharmacology teachers, most pharmacology textbooks, and even some intensive care textbooks, you will be taught how those experiments were run. After infusing known medications with known effects into a subject (usually an anesthetized animal of some kind), a researcher would then infuse a medication with an unknown effect and record what happened. The idea was that in a controlled setting, the α_1, β_1, and β_2 effect of each drug could be elucidated. You could then monitor for variations in blood pressure (both how high the pressure rose and what the pulse pressure did) and heart rate. All of that data was drawn as a tracing on paper. **That's how we found out what each drug did**. **There is no place for that in how you learn these drugs.** Props to the teams that did that work. But trying to teach it as it was discovered is preposterous. Cataloging the relative effects of each vasopressor on each of the receptors is necessary for future research. Let the PhDs doing the research learn and catalog that way. That's not how you should learn them.

We will include tracings at the end of the note set with explanations of what they mean. We will not include them in the video. We will not ask you questions about them. We will not introduce a ganglion blocker and infuse a pressor the way we did in General Pharmacology. That was truly Basic Sciences. This is Organ Systems, your bridge between the intracellular mechanisms in the Basic Sciences and actually treating another human being.

Dr. Williams's Message

No one other than those who are trained by me will communicate shock and pressors this way. If you say the word "inodilator" to an ICU attending, they are going to look at you funny. I made it up. But this is how an Internal Medicine resident viewed the ICU, crushed overnights while solo the ICU, and would fill in for the ICU fellow at 7 o'clock the next morning. When I was on, they knew they were sleeping. I'd handle it on my own. And it isn't because I had some incomprehensible capacity for the ICU. It's because I broke it down into manageable pieces. If this could get medicine residents outperforming their ICU fellows, I guarantee it is good enough for you learning this for the first time. Start with the clinical end in mind.

What Is Shock?

Shock means hypotension. When your friend in high school found out he got dumped, he was in "shock." That was not *shock* shock. On that prime-time crime drama, when someone is so paralyzed after witnessing a horrific event happen to a loved one that they can't even say a word to the po', and Olivia Benson says, *"she's in shock?"* That's not *shock* shock. When you licked that 9-volt battery on a dare in kindergarten, and you felt that little zip—that was not *shock* shock.

Real shock is defined by **insufficient perfusion of peripheral tissues**. And shock, hypoperfusion due to hypotension, is different from thrombosis (complete blockage of one artery, leading to ischemia of the distal tissue) because shock must distinctly be a global supply issue. All tissues everywhere feel it. The body has mechanisms of directing blood flow to vital visceral organs, but the damage is systemic. The large elastic arteries distend, storing systolic volume in order to recoil to provide perfusion pressure during diastole. Together, the ventricular contraction (systole) and elastic recoil of large arteries (diastole) create the mean arterial pressure. Medium arteries are conduits, and arterioles are high-resistance vessels, cranking up the resistance against the incoming perfusion pressure so that no matter what that perfusion pressure is, the capillaries behind the arteriole feel constant pressure and only the pressure they need.

Normally, proper cardiovascular function provides excess perfusion pressure such that the arterioles must rank up the resistance to prevent pressure beyond what the tissues they service need. Normally, that is about 90 mmHg of MAP and 10 mmHg of capillary hydrostatic pressure. Shock is when there is insufficient perfusion pressure to even get the blood to the arteriole. In shock, distal tissue is hypoperfused, becomes ischemic, and will die if the shock is not corrected.

The most obvious sign of overt shock is **frank hypotension**. No more systolic and diastolic pressures in the ICU, where you now are. Only MAP. A **MAP < 60 mmHg** should make you jump out of your seat and get to the bedside. A MAP goal of 60–65 is generally used to indicate a successful response to vasopressors. A MAP of 60 is low. If 120/80 is quintessential, then a MAP of 90 is normal.

Many patients are in shock but do not have frank hypotension. The older a person gets, the more sensitive this test is, but a **shock index** is the ratio of the heart rate to the systolic blood pressure. A ratio greater than 1 is suggestive of **elevated lactic acid**. In septic shock, elevated lactic acid is indicative of a poor prognosis. Lactic acid is produced by tissues that are forced to endure anaerobic metabolism—they are ischemic, deprived of oxygen and glucose. Neither the shock index nor the lactic acid is as severe as frank hypotension, but both portend a worse outcome.

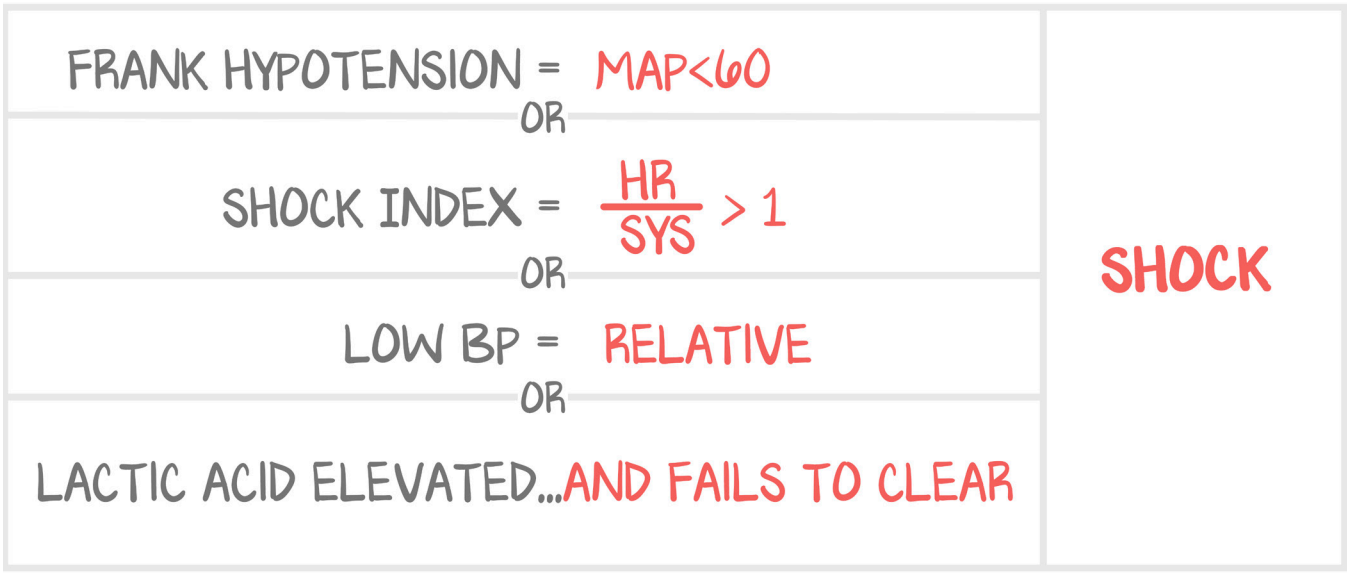

Figure 7.1: Shock Signs and Symptoms

Approach to Shock

Step 1. Is it CO or SVR?

See cardiac output as the systolic whomp. The pressure added to whatever the diastolic tone is. A good cardiac output means a taller jump in systole. See systemic vascular resistance as diastolic tone. Because SVR is the combination of all combined arterioles, it represents how tight the vessels squeeze. That is going to set the baseline diastolic pressure to which the systolic whomp is added.

Cardiac output is how high systole goes. Systemic vascular resistance is the lowest the pressure will go, diastole. Because one compensates the other, you can use the pulse pressure and skin temperature of the extremities to assess which side of the equation is broken. Use this figure to read along with the next paragraph.

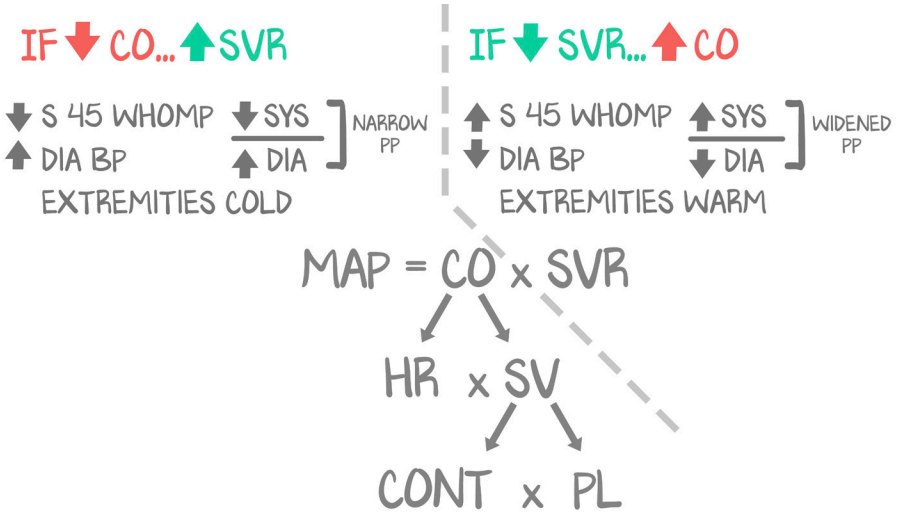

Figure 7.2: Cardiac Output Shock vs. Systemic Vascular Resistance Shock

If cardiac output is broken, systemic vascular resistance (SVR) will respond by increasing vasoconstriction. The patient is in shock, so clamping down with insufficient perfusion pressure cuts off distal extremity blood flow to preserve visceral organ perfusion. Cold shins and forearms AND hypotension suggest that systemic vascular resistance is intact and reacting to dysfunctional cardiac output. SVR is also diastole. SVR is working really hard, so the diastolic tone is high. The systolic whomp has failed. Therefore, the baseline is higher and the lift in systole is smaller. This is a narrowed pulse pressure.

Conversely, if SVR fails, the vessels will inappropriately dilate, and the cardiac output must compensate. Vasodilation means that despite low perfusion pressure, the extremities will be warm. Warm shins and forearms AND hypotension suggest that the cause is SVR. The diastolic tone will be low, and the systolic whomp will be high; diastole falls while systole rises higher. This is a widened pulse pressure.

Step 2. Which component is broken?

When a patient is hypotensive, you should take a quick trip around the MAP equation to determine what is wrong. You start at a low MAP—on the left of the equation—and work your way around counterclockwise. This is a serious exercise, not an esoteric one. When residents called me to the bedside (something I discouraged but never refused, meaning they really needed my presence) for a patient in shock, this is the exercise I would put them through. When I saw a patient in shock, this is the method I used. A low MAP means there is an insult so severe that the compensatory mechanisms have failed, or there are multiple insults at once. Always assume on your first pass of this technique that there is only one insult, and that insult is severe. Follow along with the image as the text progresses. At the end of each paragraph, come back up here and find yourself on the MAP equation, using it as a map.

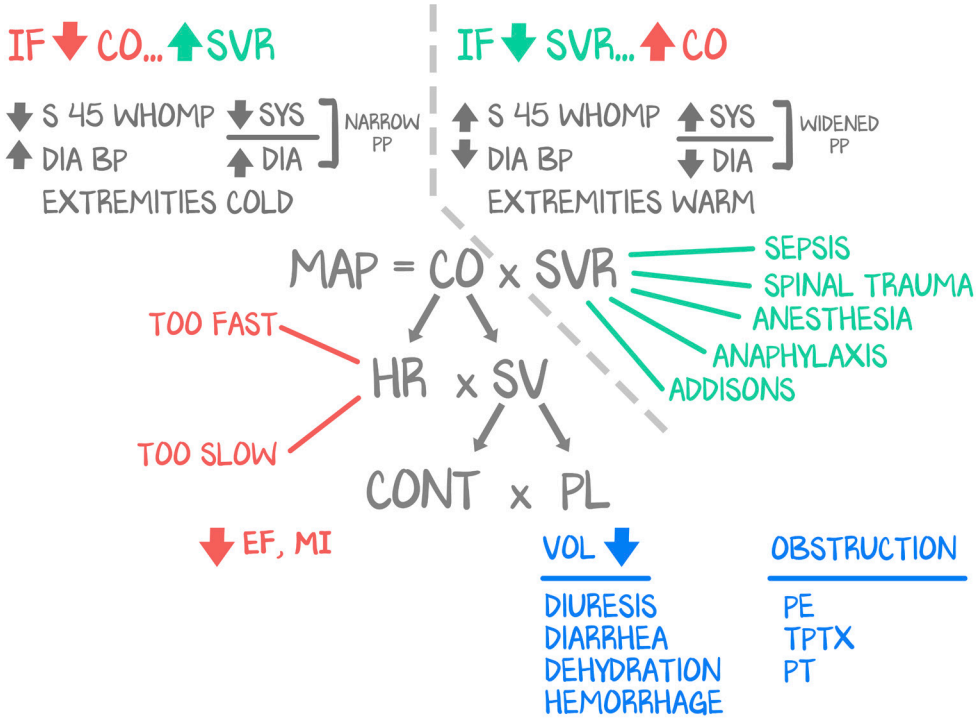

Figure 7.3: Differential for Shock Using the MAP Equation

First is **heart rate**. The only way for an arrhythmia to cause shock is for there to be an arrhythmia. Arrhythmias are either too fast or too slow and are not sinus rhythms. There should be no question whether an arrhythmia is the cause. There will be an extreme variation from normal, and the hypotension would begin with the onset of the arrhythmia. Sinus tachycardia at 130 is in response to something else, move on, find the something else. A rhythm that is too fast to see p-waves and 180 bpm with the patient lying down doing nothing is probably an arrhythmia and the problem. A patient who is asleep and asymptomatic and has good blood pressure with a heart rate of 55 is probably fine. In a patient with a heart rate of 20 and no palpable pulse except at the carotid, the bradyarrhythmia is probably causing the hypotension. Prepare for intervention (next section). But while those moves are being made, quickly assess the rest of the equation. This may not feel intuitive yet, but heart rate is the first to be encountered because it is the most obvious to detect and the one in need of the most immediate treatment (electricity, found on the crash cart).

Second is **contractility**. If the patient has a known impaired ejection fraction, fluid everywhere (JVD, crackles, peripheral edema), and evidence of poor forward flow (renal failure, encephalopathy), it may be contractility. This is the hardest to assess on the fly and generally requires further investigation. In practice, having a point-of-care ultrasound to assess the IVC and ballpark an ejection fraction is huge. If you're without one, and it isn't super obvious due to massive overload and a history of heart failure, move on and come back around after you've finished the tour of the equation. Myocardial infarction and systolic congestive heart failure are the two main players in this category.

Third is **preload**. We have said all along that **preload is volume**. You now assess the patient's volume status. You cannot adequately assess a patient's volume status with a physical exam if they are volume depleted. In children, sunken eyes, poor skin turgor, and dry mucus membranes have meaningful likelihood ratios to assess for volume depletion. In adults, especially the elderly, there is no reliable physical exam maneuver to tell you they are dry. Instead, make sure they are not wet. We've talked about preload as if it were sodium, and where sodium goes, water follows. Don't forget hemorrhage. If they are hemorrhaging, the cause of shock is preload.

However, preload can be more than volume loss. **Obstruction** of blood flow into a ventricle also counts. Limited venous return is the same thing as limited EDV, which is preload. The trouble is that you must do more for obstruction than simply replete. Pericardial tamponade (preload to the right ventricle compromised), tension pneumothorax (preload to the right ventricle compromised), and massive pulmonary embolism (preload to the left ventricle compromised) need to be considered. That's as far as we're taking this discussion at the Basic Sciences level—"need to be considered."

Fourth is **systemic vascular resistance**. The most common type of shock in a medical ICU is **septic shock**. Septic shock is due to massive vasodilation due to antigenic molecules, such as LPS. When someone is septic, they are also volume depleted. Septic patients need 30 cc/kg bolus on presentation. There is usually evidence of infection. Culture up—chest X-ray, urine, blood. Make sure they get fluid before the chest X-ray—you need an infection, neutrophils, and adequate fluid status to see consolidation. The other causes of systemic vascular resistance failure are **anesthesia** (did they just come out of the OR?), **Addisonian crisis** (relative adrenal insufficiency, known Addison's disease?), **spinal trauma**, and **anaphylaxis** (if they have wheezing and a rash, stick them with epinephrine).

Fixing Shock

The only time giving preload is a bad idea is when they already have too much. If the patient is obviously volume overloaded and you have already decided that they are in cardiogenic shock due to CHF, don't give fluids. Otherwise, an initial bolus doesn't hurt, and it might help. Whatever the problem is—depleted preload, no systemic vascular resistance, or a wonky heart rate—because everything in the MAP equation is multiplied, giving volume can temporarily compensate for the MAP. The only thing the body cannot immediately increase is preload. The neural mechanisms affect the heart rate, contractility, and blood vessels. Angiotensin 2 affects the blood vessels. Aldosterone takes hours to days to take effect. The easiest thing for you as a provider to intervene on is preload. Convenient. Give preload when it isn't obviously contraindicated.

Let's go around the MAP equation again, addressing the treatment of each element. Follow with the figure.

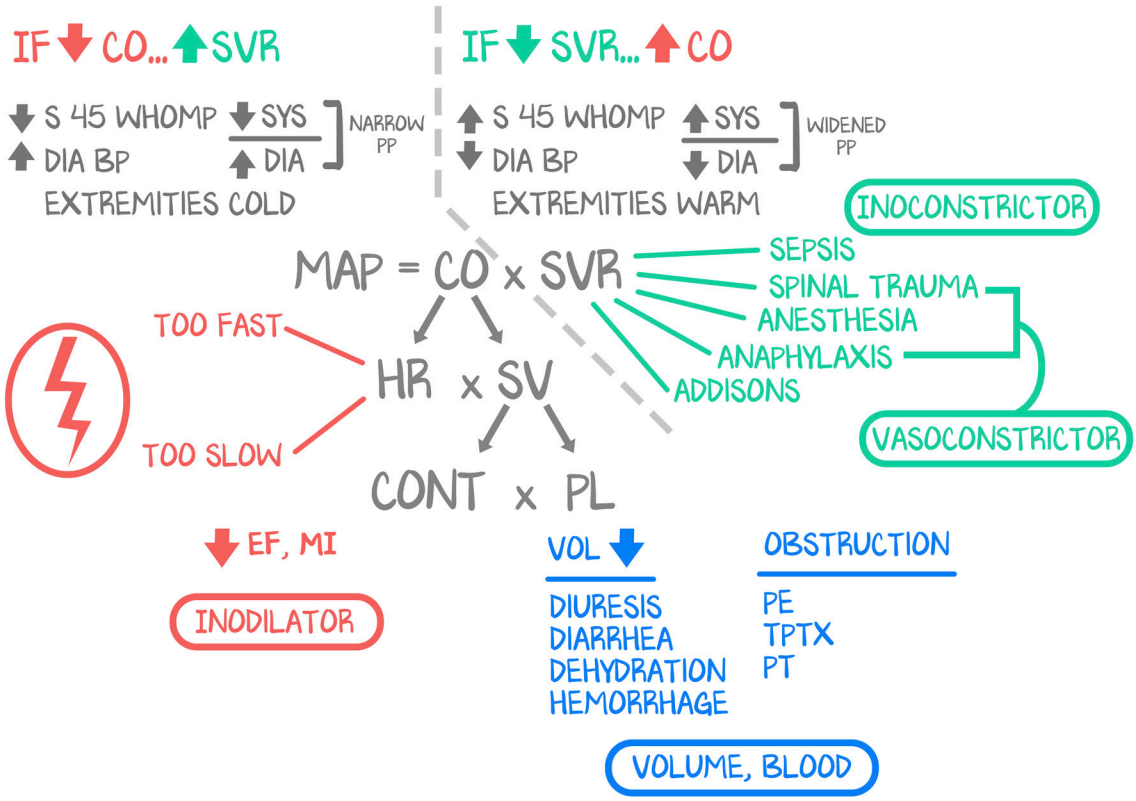

Figure 7.4: Approach to Treating Shock Using the MAP Equation

If the patient has an arrhythmia and is in shock, use **electricity**. Transcutaneous pacing for slow rhythms, synchronized cardioversion for fast rhythms. Are there medications you can give? Yes. But we started with dying tissue everywhere. This discussion begins with the need to act in minutes. If arrhythmia and shock, fix with electricity. And there has to be an arrhythmia, not just a change in heart rate out of range. Sinus tachycardia and sinus bradycardia are not arrhythmias.

Next is **contractility**. That one is hard to explain without the information on vasopressors below. You give **inodilators** for cardiogenic shock due to congestive heart failure. We'll come back to this one.

Then **preload**. If they are bleeding, the best vasopressor to use is . . . blood. Plug the hole, reverse coagulopathy, and fill them back up. We're not talking transfusion goals and all possible indications in this lesson. We will discuss that in Hematology. Right now, we're talking about someone bleeding from both ends of their GI tract faster than you can transfuse blood. If they are hypotensive because they have lost that much volume, give the volume back. Ideally, you would give what they lost—blood, platelets, plasma. But in the moment, give what you have—fluids. If it is that bad, get as many peripheral lines as you can, as large as you can. Transfusion is limited more by the length of the catheter than by the radius of the line. You did learn r^4, and that matters to arterioles. The minimum length of a central line is about 25 cm, and they can be as long as 60 cm. A 20G IV is 32 mm long. A central line is 10–20 times longer than a peripheral line (to the first power), which translates to 10–20 times more resistant than a peripheral line. A peripheral 20G is five-sixths as wide as a peripheral 18G—7 times more resistant. Multiple, short, fat peripheral lines are infinitely superior to a central line when considering blood and volume.

Finally, **systemic vascular resistance**. That one is hard, too. Either you give **inoconstrictors** for sepsis or **pure vasoconstrictors** for every other cause. We'll also come back to this one.

Heart rate shock is fixed with electricity, preload is fixed by giving preload, and the ones left over are hard. Enter vasopressors.

Pressors

What's the best pressor to use if the problem is arrhythmia? Electricity.

What's the best pressor to use if the problem is bleeding? Blood.

What's the best pressor to use if the problem is cholera diarrhea? Saline.

We're running out of indications . . .

Use this illustration to follow along with the text:

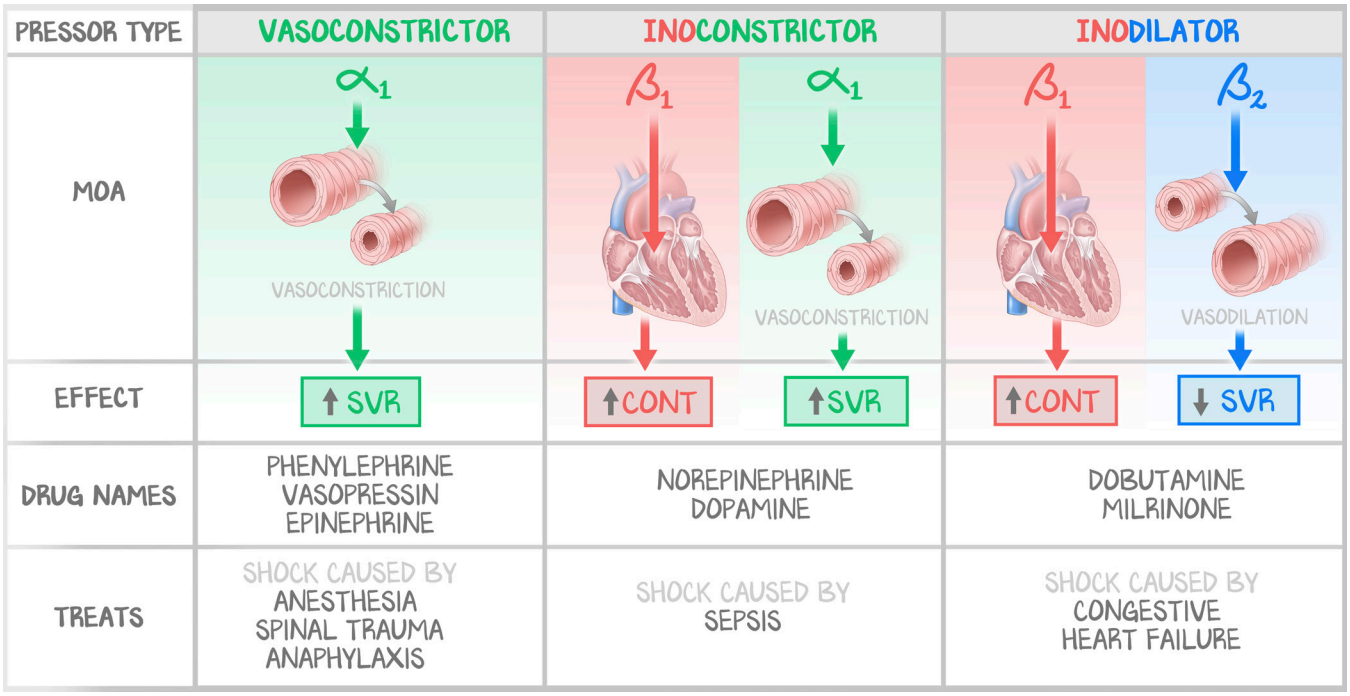

Figure 7.5: Pressors à la Dr. Williams

Enter the educational wizardry of Dustyn Williams. A word of caution, though. Repeat this amongst your friends. Use these terms in group, in cases, and even with the patients that you get to make decisions on during your rotations. But be careful saying it out loud and whom you say it around. If you do say it to people who are unfamiliar with it, make sure to preface that it's just how you learned it and how it made sense to you. These are Dustynisms and are not common language in pulmonary critical care. This is also something that, until this lesson, OME considered appropriate only for M4s transitioning to PGY-1. After looking over this material while building the Basic Sciences, we realized that there was no good reason to withhold it and subject you to the garbage method we were subjected to, which forced this approach to vasopressors to be created in the first place.

So, here we go. There are four types of pressors: pure vasoconstrictors (α_1 only), inoconstrictors (β_1, α_1), inodilators (β_1, β_2), and pure vasodilators (the infused antihypertensive medications that lower blood pressure, so they are obviously not useful for treating shock).

Pure **vasoconstrictors** are used to treat dysfunctions of systemic vascular resistance caused by anything other than sepsis. There is no chronotropic support or inotropic support to the heart, which means that the only problem must be vasoconstriction. That happens with anesthesia, trauma to the spine, and anaphylaxis. The commonality is either a temporary loss of neural signaling or a signal that overpowers the endogenous norepinephrine activation of α_1. α_1-Only drugs yell at the blood vessels to constrict. Drugs in this class are **phenylephrine**, **vasopressin**, and **epinephrine**. Put an asterisk by epinephrine, as it's more complicated than I'd like it to be. Epinephrine stimulates α_1, β_1, and β_2 receptors. But when you reach for epinephrine as a treatment for shock, you are giving it for its α_1 properties. When you use epinephrine to correct anaphylaxis (which causes death due to hypotension, not airway swelling as in the movies) or as a third infused medication as an adjunct to other agents for septic shock, you are using it for its α_1 properties. This is the biggest fudge of the organizer, and we'll talk epinephrine in detail later this lesson.

The **inoconstrictors** combine inotropic support (ino, β_1) with vasoconstriction (constrictor, α_1). These medications are the ones used to treat **septic shock**. Although **norepinephrine** is preferred over **dopamine** (because of minor arrhythmia side effects that you shouldn't concern yourself with at this stage), either is appropriate for septic shock. The first step, as soon as you identify sepsis, is to fix the volume status. *"If septic, then volume depleted."* Tachypnea and fever alone can cause volume depletion, not to mention the decreased oral intake associated with being ill. If the bolus of fluid corrects the blood pressure and alleviates the elevated lactic acid, no pressor may be needed. A failure to clear the lactate or persistent hypotension after fluid resuscitation necessitates inoconstrictor support. What comes after that is, again, not for your level of training.

The **inodilators** combine inotropic support (ino, β_1) with systemic vasodilation (dilator, β_2). These medications are used to treat **contractility shock**. That's another made-up word. "Contractility shock" is "cardiogenic shock due to a depressed ejection fraction." Cardiogenic shock, outside OME and Dustyn Williams's practice pattern, means something else entirely (see the next section). In contractility shock, the heart isn't strong enough to resist afterload (stimulation). The problem with heart failure shock (contractility shock) is that the body's response to low blood pressure (baroreceptors) and poor tissue perfusion (kidneys) is to clamp down on the vasculature, to increase the afterload. Then, an already failing heart is asked to contract against increased systemic vascular resistance with excess preload. The β_1 gives the boost to fight back. Nothing can be done about the angiotensin 2 vasoconstriction, but stimulation of β_2 receptors vasodilates skeletal muscle arteries, thereby reducing afterload. The suppressed ejection fraction gains the benefit of extra contractility delivered by the ino- part (β_1), whereas the excess vasoconstriction is alleviated by the -dilator part (β_2).

Below this point is for reference. We cover a practical approach to shock and shock treatment above. Below are the details that you could learn but aren't necessary.

The Real Stuff and Test Prep

There are four traditional buckets of shock—distributive, cardiogenic, obstructive, and hypovolemic.

Distributive shock is what I call "systemic vascular resistance shock." It is just a different name, but it fits our model.

Cardiogenic shock, in the traditional model, could mean **either** contractility shock or heart rate shock. I do not endorse learning that way because although both heart failure and arrhythmia are indeed problems with the heart (cardiogenic), the word cardiogenic doesn't tell you what you should do. Do you shock them or start dobutamine? That is why I recreated the approach to shock the way I did.

Two types of traditional shock both fall under what I call "preload shock"—hypovolemic and obstructive. **Hypovolemic shock** (usually in the context of hemorrhage) and **obstructive shock** (pulmonary embolism, tamponade, tension pneumo) are separate entities based on the same thing.

This is a peculiar thing I ask of you—learn it my way, but also how to say it the traditional way. You may embarrass yourself before your attending when you repeat an uncouth Dustynism and save a life by making the right call. But isn't a little embarrassment a small price to pay for saving a life?

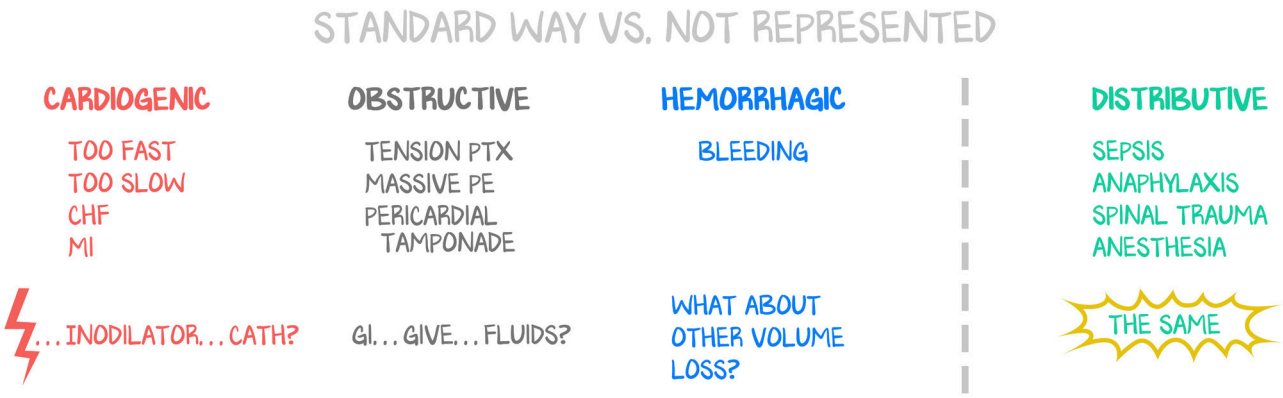

Figure 7.6: Causes of Shock via the Traditional Method (and Pitfalls)

Dopamine

Dopamine infusions have a dose-dependent effect. Dopamine can stimulate dopamine receptors, β_1 receptors, and α_1 receptors. The **dopamine receptor** effect predominates at low rates (< 5 mcg/kg/min), the **β_1 receptor** effect predominates at moderate rates (5–10 mcg/kg/min), and the **α_1 receptor** effect predominates at high rates (> 10 mcg/kg/min).

Dopamine receptor activation was once thought to cause renal artery dilation and to improve kidney perfusion. This was thought because putting a patient who is oliguric on dopamine improved urinary output. It was presumed that because there was more urine output, there was more glomerular filtration and, therefore, more renal perfusion. However, **dopamine receptors induce diuresis**, not improved renal perfusion.

Both α_1 and β_1 receptors are activated at all doses. Dopamine is titrated to effect. In the use of dopamine in treating septic shock, β_1 receptor activation can provide a little inotropic support, but it also **causes arrhythmias**. Norepinephrine also stimulates α_1 and β_1. Norepinephrine tends to cause fewer arrhythmias, but dopamine and norepinephrine are both considered equivalent as the first agent for treating septic shock.

Epinephrine

Epinephrine activates α_1, β_1, and β_2 receptors. Epinephrine the hormone and epinephrine the drug act the same way. Everything you learned about epinephrine in General Pharmacology is true of the drug. We're going to talk here about the practical applications of the drug.

Because of α_1 stimulation, the blood pressure increases. Because of β_1 stimulation, the heart rate increases. Because of β_2 stimulation, systemic vascular resistance decreases. Those words were chosen on purpose. α_1 Makes the MAP higher, makes the systolic blood pressure higher, makes the diastolic blood pressure higher. β_2 Causes a decrease in systemic vascular resistance, decreasing the diastolic blood pressure. That widens the pulse pressure while still increasing the MAP.

Epinephrine can be administered at lower infusion rates to provide **chronotropic** support in bradycardia. At small doses, the effect on heart rate predominates over the systemic effects.

Epinephrine is administered as an **intramuscular injection** to treat **anaphylaxis**. Although anaphylaxis does cause airway collapse via bronchoconstriction, and epinephrine's activation of β_2 induces bronchodilation, that isn't how epinephrine saves. In anaphylaxis, there is massive systemic vasodilation. The stimulation of α_1 receptors restores the MAP while also having the added benefit of opening the airways.

Epinephrine is administered at higher infusion rates in the treatment of **septic shock**. Norepinephrine is first. Then vasopressin is added second. Epinephrine is added as a third agent before corticosteroids. The requirement of a third pressor portends a dismal prognosis.

Waveforms and Tables

AGENT	α_1	α_2	β_1	β_2	D1
Dobutamine	+	+	++++	++	0
Dopamine	++	0	++++	++	++++
Epinephrine	++++	++++	++++	+++	0
Norepinephrine	+++	+++	+++	+/++	0
Phenylephrine	+++	-	-	-	-

Table 7.1

How to interpret these waveforms. If the blood pressure goes up, the whole tracing goes up. The top of the tracing is systolic pressure, and the bottom is diastolic pressure. Systole is dependent on contractility, and diastole is dependent on systemic vascular resistance. Systemic vascular resistance goes up with α_1 activation and down with β_2 activation. Both control the diastolic pressure. The more up-and-down zigzags there are, the faster the heart rate. The fewer there are, the slower the heart rate.

α_1 Only. Phenylephrine is purely α_1. When given to an animal in the laboratory, phenylephrine causes systemic vascular resistance to increase, so the diastolic pressure rises. There is no change in heart rate or contractility due to the medication, so the pulse pressure doesn't change. The MAP is higher. In the laboratory, phenylephrine also results in bradycardia and a narrowed pulse pressure. As the MAP goes up, the baroreceptor reflex is activated. There is an increase in parasympathetics and a decrease in sympathetics. The heart rate slows, and contractility goes down (loses its stimulus, but same effect).

β_1 Only. No medication is only a β_1 agonist. In theory, stimulating only β_1 would increase heart rate and contractility. The increased contractility leads to a widened pulse pressure and higher systolic pressure. The baroreceptors would sense the slightly increased systolic pressure, leading to a decrease in sympathetic tone, which would reduce systemic vascular resistance. Overall, the diastolic pressure does not change, but the systolic pressure does.

β_2 Only. There are no purely β_2 agonists. In theory, if there were only β_2 agonism, systemic vascular resistance and diastolic pressure would both decrease. There would be no change in contractility, so the pulse pressure would remain the same. With the falling blood pressure, baroreceptors would increase sympathetic tone. That sympathetic tone would provide contractility (widening the pulse pressure) and tachycardia (more zig-zags).

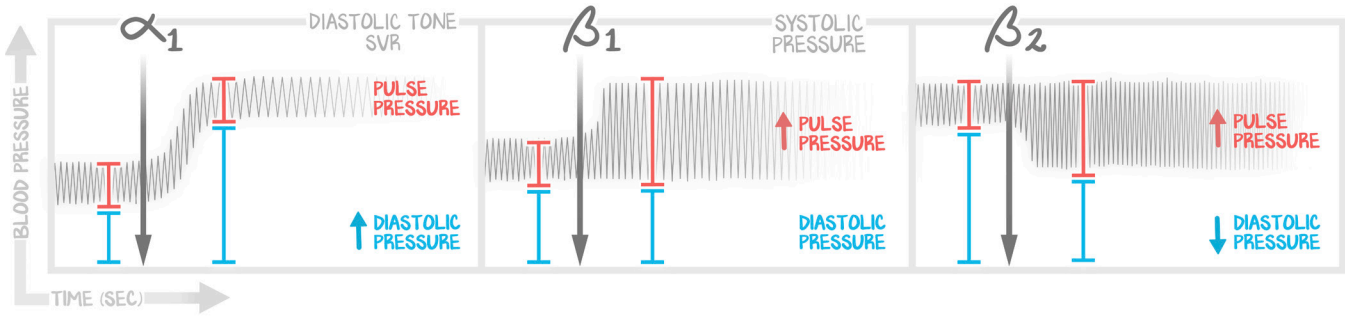

Figure 7.7:

β_1 And β_2 together. Isoproterenol was the nonselective β agonist used in animal studies. It is the prototypical drug for dobutamine and milrinone. When β_1 receptors are activated, the heart rate and contractility increase, thus increasing the MAP. But very quickly thereafter, β_2 activation (the reduction in systemic vascular resistance) wins, and although the heart rate remains elevated, the blood pressure falls to well below the original pressure. The falling pressure disinhibits the baroreceptor reflex and the endogenous sympathetic output increases. β_1 And α_1 are activated, and the systolic pressure rises. The diastolic pressure (driven by β_2 in skeletal muscle) stays low. This experiment is what trips up people managing heart failure in the ICU. They learn in school that isoproterenol causes a drop in blood pressure because of β_2 stimulation, and when confronted with cardiogenic shock, they are reluctant to give dobutamine. Isoproterenol causes a transient drop in blood pressure when applied to anesthetized, healthy animals. Dobutamine is given to patients with a massively increased systemic vascular resistance, driven by both angiotensin 2 and the sympathetic nervous system. Dobutamine both gives the failing heart a boost (β_1) and undoes the damage being done by angiotensin 2 (β_2).

α_1, β_1, and β_2. Epinephrine is the "nonselective sympathomimetic." It activates all adrenergic receptors. Because of β_1 stimulation, the contractility and, subsequently, the systolic blood pressure and pulse pressure increase. Because of β_1, the heart rate increases. Because of α_1 stimulation, the systemic vascular resistance increases, so the diastolic pressure increases. But only initially. Because of β_2 stimulation, the systemic vascular resistance falls, and the diastolic pressure goes down. The competition of β_2 and α_1 overall leads to an increase in the diastolic pressure.

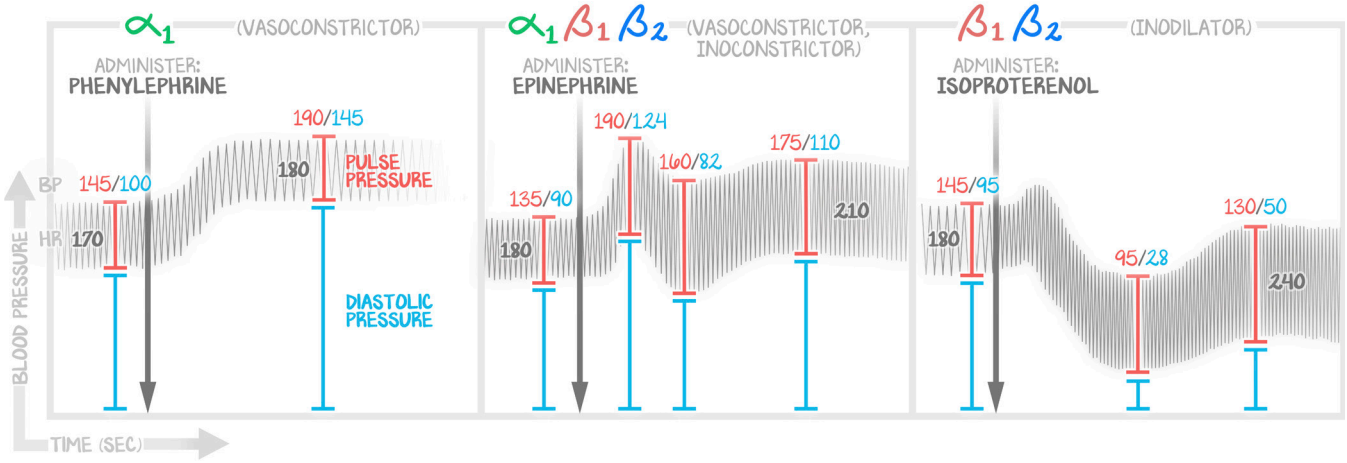

Figure 7.8: